

### **REMARKS/ARGUMENTS**

With this amendment, claims 1-33 are pending. Claims 2-6 and 8-23 are canceled. For convenience, the Examiner's rejections are addressed in the order presented in an October 6, 2003, Office Action.

#### **I. Clarification of restriction/election of species**

Applicants affirm election of the following species by telephone on September 16, 2003: Claim 28, a Cullin protein; Claim 30, SCF; Claim 31,  $\beta$ -TRCP, and Claim 33, Skp1.

#### **II. Claim objections**

Claim 1 is objected to as being a substantial duplicate of claim 7. Applicants respectfully traverse the objection. Claim 1 is directed to isolated and purified biologically active ring box proteins, *e.g.*, naturally occurring or recombinant Ring box proteins. Claim 7 is directed to recombinant ring box proteins and is thus a subset of the proteins of claim 1. Therefore, claims 1 and 7 are not substantial duplicates. In view of the above arguments, Applicants respectfully request that the objection be withdrawn.

#### **III. Rejections under 35 U.S.C. §102(b)**

##### ***A. Introduction***

Claims 1, 7, and 24-33 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Daum *et al.*, (PNAS, 92:6459-6463 (1995)) as further evidenced by Pause *et al.* (PNAS, 94:2156-2161 (1997)). The Office Action alleges that Daum *et al.* inherently anticipates the claimed invention because it discloses an uncharacterized 16 kDa protein.

Applicants respectfully traverse the rejection. The claimed invention is an isolated and purified Ring box protein with an amino acid sequence of SEQ ID NO:1. The claimed Ring box protein has a molecular weight of approximately 16 kDa. Protein complexes comprising the Ring box protein are also claimed.

In contrast, neither of Daum *et al.* nor Pause *et al.* provide the amino acid sequence of the claimed Ring box protein. Daum *et al.* all disclose only the amino acid and nucleotide sequences of rat and human VHL proteins. Daum *et al.* disclose proteins that immunoprecipitate with VHL proteins, including a 16 kDa protein band that immunoprecipitated with VHL. The 16 kDa band is actually a triplet, indicating more than one protein is present in the band. (Daum *et al.* at page 6460, column 2.) Daum *et al.* provides no other characterization of the 16 kDa protein band and provides no amino acid sequence of any 16 kDa protein, including the claimed sequence. The second reference cited, Pause *et al.*, also fails to disclose the sequence of the claimed Ring box protein and fails to disclose a protein complex that includes a Ring box protein. Pause *et al.* discloses only protein complexes formed by VHL, and, in fact, discloses VHL complexes comprising low molecular proteins that are not Ring box proteins. (See, *e.g.*, Pause *et al.*, Figure 5 at page 2160.) Thus, Pause *et al.* provides evidence that the low molecular weight proteins of Daum *et al.* are not necessarily the claimed Ring box proteins.

*B. The cited references to not provide an enabling disclosure of the claimed Ring box proteins.*

An allegedly anticipatory reference must enable the subject matter that it is asserted to anticipate. *Elan Pharmaceuticals v. Mayo Foundation for Medical Education and Research*, 68 USPQ2D 1373, 1375 (Fed. Cir. 2003). Merely naming or describing the desired subject matter is not sufficient for an enabling disclosure if undue experimentation is required to produce it. *Id.* at 1376.

The claimed invention is a Ring box polypeptide with a specific amino acid sequence, *i.e.*, a chemical compound. Courts have developed a body of case law regarding the information required to provide an enabling disclosure of a chemical compound. In order to place a chemical compound in possession of the public, the disclosure must be such that one of ordinary skill in the art could at once envisage the structure of the compound. *In re Donohue*, 207 USPQ 196, 199 (Fed Cir. 1980) and *In re Petering*, 133 USPQ 275, 279-280 (C.C.P.A.

1962). In addition, the reference must disclose a method of making the compound. *Hoeksema*, 158 USPQ at 601.

The Federal Circuit has ruled that for genetic material, one of skill cannot visualize or recognize the a genus unless a DNA sequence or other common structural feature is provided. *See, e.g., University of California v. Eli Lilly*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). By analogy, for a polypeptide such as the claimed Ring box protein, the required chemical structure is the amino acid sequence. Because neither of the cited references discloses the amino acid sequence of the claimed Ring box protein, one of skill would not be able to at once envisage the compound based on those disclosures. Thus, the cited references do not provide an enabling disclosure and are not properly cited as prior art.

Daum *et al.* and Pause *et al.* also fail to enable the claimed inventions because the references do not provide a method of making the claimed Ring box proteins. The Federal Circuit has provided a legal standard for information necessary to conceive a method of making a nucleic acid, *i.e.*, the information necessary to disclose a method of making a nucleic acid and, by analogy, a method of making a protein. According to the Federal Circuit, both conception of a nucleic acid (or protein) structure and a method of making a nucleic acid (or protein) occur simultaneously with disclosure of the DNA (or amino acid) sequence. *See Amgen v. Chugai*, 927 F.2d 1200 (Fed. Cir. 1991); *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993); *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993); and *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995). Thus, in order to disclose a method of making a specific protein, a specific amino acid sequence must be provided.

As indicated above, neither Daum *et al.* nor Pause *et al.* provide the amino acid sequence of the claimed ring box protein. Because the references do not provide a specific amino acid sequence, they do not disclose a method of making the claimed Ring box proteins and thus, are not enabling references.

C. *The cited references do not expressly or inherently disclose the claimed Ring box proteins.*

To anticipate a claim, either expressly or inherently, a reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the

claim is found...in a single prior art reference.” *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Thus, in order to anticipate, the cited references must contain every element of the claims at issue.

The Office Action alleges that the 16 kDa protein of Daum and the claimed Ring box protein are identical, apparently because they have similar molecular weights. As the Examiner knows, proteins with different amino acid sequences can have similar molecular weights. Thus, in the absence of sequence information, similarity of molecular weight does not indicate that two proteins are identical. Daum *et al.* does not disclose the amino acid sequence of a Ring box protein and thus, does not contain each element of the claimed invention. In addition, the 16 kDa band is a triplet, and thus does not disclose the isolated and purified Ring box protein required by the claims. (Daum *et al.* at page 6460, column 2.) Pause *et al.* also fails to disclose the amino acid sequence of the Ring box protein. Therefore, the cited references do not expressly anticipate the claimed invention.

With regard to inherent anticipation of a particular feature, an undisclosed element anticipates only if it is necessarily present in the cited reference. *Schering Corp. v. Geneva Pharmaceuticals, Inc.* 67USPQ2d 1664, 1667 (Fed. Cir. 2003), citing *Continental Can Co. v. Monsanto Co.* 20 USPQ2d 1746 (Fed. Cir. 1991). However, the claimed Ring box protein is not necessarily a component of VHL protein complexes disclosed in either Daum *et al.* or Pause *et al.*

The Office Action alleges that Pause *et al.* teach protein complexes comprising VHL and the claimed Ring box protein and thus, provides evidence of inherent disclosure of the claimed subject matter by Daum *et al.* Although, Pause *et al.* demonstrate that the VHL protein forms complexes with a cullin protein and elongins B and C, Pause *et al.* do not provide any evidence that Ring box protein is present in such complexes. In fact, Pause *et al.* provide evidence that, in the absence of Ring box protein, VHL is able to form complexes with low molecular weight proteins Elongin B and C. (See, *e.g.*, Pause *et al.*, Figure 5 at page 2160.) Therefore, Pause *et al.* provide evidence that the complexes of Daum *et al.* do not necessarily include the claimed Ring box protein, and thus Daum *et al.* does not inherently disclose the claimed invention.

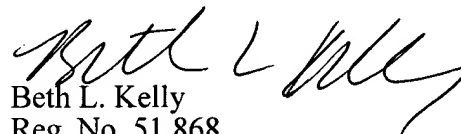
In view of the above arguments, Applicants respectfully request that the rejection under 35 U.S.C. §102(b) be withdrawn.

**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

  
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